

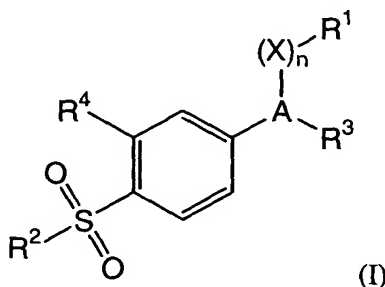
WHAT IS CLAIMED IS:

1. A composition comprising gelatin and an amine agent that comprises at least one pharmaceutically acceptable primary or secondary amine, the composition being suitable for preparation of a pharmaceutical capsule shell.
2. The composition of Claim 1 wherein the amine agent is present in an amount effective to inhibit cross-linking of the gelatin and/or pellicle formation in a capsule shell prepared from the composition.
3. The composition of Claim 1 wherein the amine agent comprises a compound selected from the group consisting of tromethamines, ethanolamine, ethylenediamine, diethylamine, ethylene N-methyl-D-glucamine, amino acids, diethanolamine, benethamine, benzathine, piperazine, hydrabamine, and imidazoles.
4. The composition of Claim 1 wherein the amine agent is present in an amount of not more than about 10% of the composition on a dry weight basis.
5. The composition of Claim 1 wherein the amine agent is present in an amount of not more than about 5% of the composition on a dry weight basis.
6. The composition of Claim 1 wherein the amine agent is present in an amount of not more than about 2% of the composition on a dry weight basis.
7. The composition of Claim 1 further comprising at least one excipient selected from the group consisting of decomposition inhibitors, opacifying agents, preservatives and plasticizers.
8. The composition of Claim 1 further comprising a plasticizer selected from the group consisting of polyhydroxy-alcohols, esters of polyhydroxy-alcohols, dialkylphthalates, lower alkyl citrates wherein the lower alkyl has 1 - 6 carbon atoms, glycols, polyglycols, ricinoleic acid and ricinoleic acid esters.
9. The composition of Claim 1 further comprising a plasticizer selected from the group consisting of sorbitol, glycerol, propylene glycols and polyethylene glycols.

10. The composition of Claim 1 further comprising a preservative selected from the group consisting of methylparabens, propylparabens, butylparabens, sorbic acid, benzoic acid, editic acids, phenolic acids, sorbates, and propionates.
11. The composition of Claim 1 further comprising titanium dioxide.
12. The composition of Claim 1 further comprising sulfur dioxide.
13. The composition of Claim 1 that is in a form of capsule shells.
14. The composition of Claim 13 wherein each of said capsule shells defines a fill volume.
15. The composition of Claim 13 wherein the capsule shells are soft gelatin capsule shells.
16. The composition of Claim 14 wherein the fill volume has a capacity of about 0.1 ml to about 2 ml.
17. The composition of Claim 16 wherein the fill volume has a capacity of not more than about 1 ml.
18. The composition of Claim 14 wherein the capsule shells are suitable for oral delivery of a drug contained in the fill volume.
19. A pharmaceutical dosage form comprising a fill material sealed in capsule shells, wherein the capsule shells comprise gelatin and an amine agent that comprises at least one pharmaceutically acceptable primary or secondary amine, and wherein said amine agent is present in an amount sufficient to inhibit gelatin cross-linking and/or pellicle formation in the gelatin capsule shells upon storage of the dosage form.
20. The dosage form of Claim 19 wherein the fill material is liquid.
21. The dosage form of Claim 20 wherein the fill material is self-emulsifying upon contact with gastric fluid.
22. The dosage form of Claim 19 wherein the fill material comprises an amine agent comprising at least one pharmaceutically acceptable primary or secondary amine

wherein the amine agent in the fill material is present in an amount effective, in combination with the amine agent in the capsule shell, to inhibit gelatin cross-linking and/or pellicle formation in the capsule shell upon storage of the dosage form.

23. The dosage form of Claim 19 wherein the fill material comprises a pharmaceutically acceptable sulfite compound in an amount effective, in combination with the amine agent in the capsule shell, to inhibit gelatin cross-linking and/or pellicle formation in the capsule shell upon storage of the dosage form.
24. The dosage form of Claim 19 wherein the fill material comprises a drug.
25. The dosage form of Claim 24 wherein the drug is of low water solubility.
26. The dosage form of Claim 24 wherein the drug is a selective cyclooxygenase-2 inhibitory drug.
27. The dosage form of Claim 26 wherein the selective cyclooxygenase-2 inhibitory drug is a compound of formula (I)



wherein:

A is a substituent selected from partially unsaturated or unsaturated heterocyclyl and partially unsaturated or unsaturated carbocyclic rings, preferably a heterocyclyl group selected from pyrazolyl, furanonyl, isoxazolyl, pyridinyl, cyclopentenonyl and pyridazinonyl groups;

X is O, S or CH<sub>2</sub>;

n is 0 or 1;

R<sup>1</sup> is at least one substituent selected from heterocyclyl, cycloalkyl, cycloalkenyl and aryl, and is optionally substituted at a substitutable position with

one or more radicals selected from alkyl, haloalkyl, cyano, carboxyl, alkoxy carbonyl, hydroxyl, hydroxyalkyl, haloalkoxy, amino, alkylamino, arylamino, nitro, alkoxyalkyl, alkylsulfinyl, halo, alkoxy and alkylthio;

$R^2$  is methyl, amino or aminocarbonylalkyl;

$R^3$  is one or more radicals selected from hydrido, halo, alkyl, alkenyl, alkynyl, oxo, cyano, carboxyl, cyanoalkyl, heterocycloxy, alkyloxy, alkylthio, alkylcarbonyl, cycloalkyl, aryl, haloalkyl, heterocyclyl, cycloalkenyl, aralkyl, heterocyclalkyl, acyl, alkylthioalkyl, hydroxyalkyl, alkoxy carbonyl, arylcarbonyl, aralkylcarbonyl, aralkenyl, alkoxyalkyl, arylthioalkyl, aryloxyalkyl, aralkylthioalkyl, aralkoxyalkyl, alkoxyaralkoxyalkyl, alkoxy carbonylalkyl, aminocarbonyl, aminocarbonylalkyl, alkylaminocarbonyl, N-arylaminocarbonyl, N-alkyl-N-arylaminocarbonyl, alkylaminocarbonylalkyl, carboxyalkyl, alkylamino, N-aryl amino, N-aralkyl amino, N-alkyl-N-aralkyl amino, N-alkyl-N-aryl amino, aminoalkyl, alkylaminoalkyl, N-aryl aminoalkyl, N-aralkyl aminoalkyl, N-alkyl-N-aralkyl aminoalkyl, N-alkyl-N-aryl aminoalkyl, aryloxy, aralkoxy, arylthio, aralkylthio, alkylsulfinyl, alkylsulfonyl, aminosulfonyl, alkylaminosulfonyl, N-arylaminosulfonyl, arylsulfonyl and N-alkyl-N-arylaminosulfonyl,  $R^3$  being optionally substituted at a substitutable position with one or more radicals selected from alkyl, haloalkyl, cyano, carboxyl, alkoxy carbonyl, hydroxyl, hydroxyalkyl, haloalkoxy, amino, alkylamino, arylamino, nitro, alkoxyalkyl, alkylsulfinyl, halo, alkoxy and alkylthio; and

$R^4$  is selected from hydrido and halo.

28. The dosage form of Claim 26 wherein the selective cyclooxygenase-2 inhibitory drug is selected from the group consisting of celecoxib, deracoxib, valdecoxib, rofecoxib, etoricoxib, 2-(3,5-difluorophenyl)-3-[4-(methylsulfonyl)phenyl]-2-cyclopenten-1-one, 2-(3,4-difluorophenyl)-4-(3-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3-(2H)-pyridazinone, and pharmaceutically acceptable salts and prodrugs thereof.
29. The dosage form of Claim 26 wherein the selective cyclooxygenase-2 inhibitory drug is celecoxib.
30. The dosage form of Claim 24 wherein the fill material further comprises at least

one substance that promotes cross-linking of gelatin when in contact therewith, said substance being the drug or an excipient substance, and said substance acting independently or in combination with one or more other substances to promote said cross-linking.

31. The dosage form of Claim 30 comprising a first and a second of said capsule shells, said first and second capsule shells being substantially identical; wherein upon
- (a) testing a first capsule shell in a first *in vitro* dissolution assay;
  - (b) storing a second capsule shell in a closed container maintained at 40 °C and 85% relative humidity for a period of four weeks; and, after said storage,
  - (c) testing the second sealed capsule shell in a second *in vitro* dissolution assay which is substantially identical to the first *in vitro* dissolution assay;
- the amount of drug dissolved at 45 minutes in the second dissolution assay is within  $\pm 15$  percent of the amount of drug dissolved at 45 minutes in the first dissolution assay; and wherein the first *in vitro* dissolution assay is conducted within a reasonably short time after preparation of the composition.